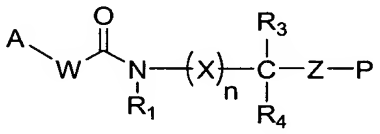
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of the claims and listing of the claims in the application:

1. (Currently Amended) A compound of Formula I,



(I)

wherein

A is a Met-AP2 inhibitory core;

W is O or NR_2;

R_1 and R_2 are each, independently, hydrogen or alkyl;

X is alkylene or substituted alkylene;

n is 0 or 1;

R_3 and R_4 are each, independently, substituted alkyl, substituted aryl or substituted or unsubstituted heteroaryl; or R_3 and R_4, together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or R_3 and R_4 together form an alkylene group;

Z is -C(O)-, alkylene or alkylene-C(O)-; and

P is a peptide comprising from 1 to about 100 amino acid residues attached at its amino terminus to Z or a group OR_5 or $N(R_6)R_7$, wherein

R_5, R_6 and R_7 are each, independently, hydrogen, alkyl, substituted alkyl, azacycloalkyl or substituted azacycloalkyl; or R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic ring structure;

or

Z is -O-, $-NR_8$-, alkylene-O- or alkylene-NR_8-, where R_8 is hydrogen or alkyl; and

P is hydrogen or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z; wherein

the N-terminus of the peptide is ~~$-NR_2R_3$~~ $-NR_2'R_3'$, wherein ~~R_2~~ R_2' is hydrogen, alkyl or arylalkyl and ~~R_3~~ R_3' is hydrogen, alkyl, arylalkyl or acyl.

2. (Currently Amended) The compound of claim 1, wherein at least one of ~~R_1,~~ R_3 and R_4 is a substituted ~~or unsubstituted~~ alkyl group.

3. (Currently Amended) The compound of claim 2, wherein at least one of ~~R_1,~~ R_3 and R_4 is a substituted ~~or unsubstituted~~ normal, branched or cyclic C_1-C_6 alkyl group.

4. (Currently Amended) The compound of claim 3, wherein at least one of ~~R_1,~~ R_3 and R_4 is a normal or branched C_1-C_4 alkyl group.

5. (Currently Amended) The compound of claim 1, wherein one of R_3 and R_4 is a substituted ~~or unsubstituted~~ aryl group, a substituted or unsubstituted heteroaryl group, a substituted or unsubstituted heteroarylalkyl group, ~~or a substituted or unsubstituted aryl alkyl group~~.

6. (Currently Amended) The compound of claim 5, wherein one of R_3 and R_4 is selected from the group consisting of ~~phenyl, naphthyl,~~ indolyl, imidazolyl, pyridyl, ~~benzyl, naphthylmethyl~~, indolylmethyl, imidazolylmethyl and pyridylmethyl.

7. (Original) The compound of claim 1, wherein n is 1 and X is C_1-C_6-alkylene.

8. (Original) The compound of claim 7, wherein X is methylene or ethylene.

9. (Original) The compound of claim 1, wherein Z is C_1-C_6-alkylene-C(O)-.

10. (Original) The compound of claim 9, wherein Z is methylene-C(O)- or ethylene-C(O)-.

11. (Previously Presented) The compound of claim 1, wherein at least one of R_6 and R_7 is alkyl, substituted alkyl, substituted or unsubstituted azacycloalkyl or substituted or unsubstituted azacycloalkylalkyl.

12. (Original) The compound of claim 11, wherein at least one of R_6 and R_7 is an azacycloalkyl group having an N-alkyl substituent.

13. (Original) The compound of claim 12, wherein the N-alkyl substituent is a C_1-C_4-alkyl group.

14. (Original) The compound of claim 13, wherein the N-alkyl substituent is a methyl group.

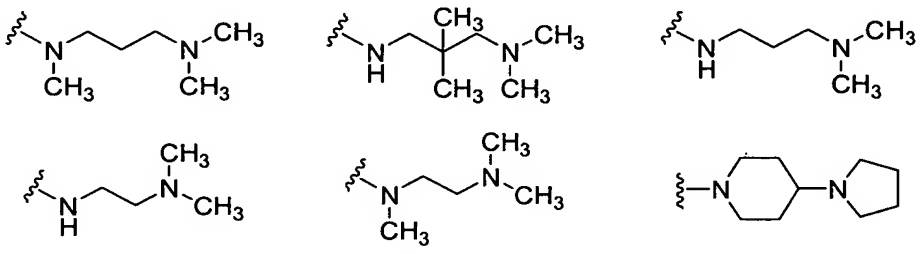
15. (Original) The compound of claim 1, wherein R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted five or six-membered aza- or diazacycloalkyl group.

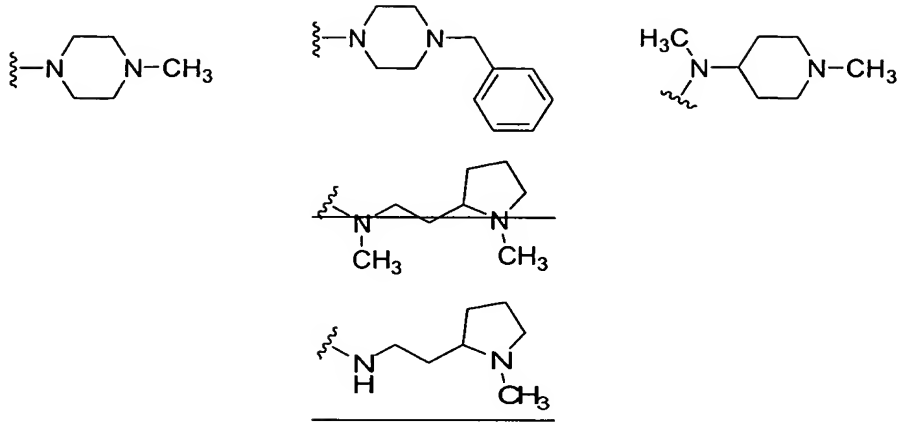
16. (Original) The compound of claim 15, wherein R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted five or six-membered diazacycloalkyl group which includes an N-alkyl substituent.

17. (Original) The compound of claim 16, wherein the N-alkyl substituent is a C_1-C_4-alkyl group.

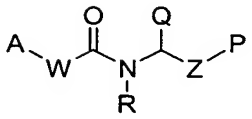
18. (Original) The compound of claim 17, wherein the N-alkyl substituent is a methyl group.

19. (Currently Amended) The compound of claim 1, wherein P is NH_2 or one of the groups shown below:





20. (Currently Amended) A compound of Formula XV,



(XV)

wherein

A is a MetAP-2 inhibitory core;

W is O or NR;

each R is, independently, hydrogen or alkyl;

Z is –C(O)- or -alkylene-C(O)-;

P is NHR, OR or a peptide consisting of one to about one hundred amino acid residues connected at the N-terminus to Z;

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is –OR, Q is not hydrogen;

or

Z is–alkylene-O-or –alkylene-N(R)-;

P is hydrogen or a peptide consisting of from one to about one hundred amino acid residues connected to Z at the carboxyl terminus; wherein

the N-terminus of the peptide is ~~$-NR_2R_3$~~ $-NR_2'R_3'$ wherein ~~R_2~~ R_2' is hydrogen, alkyl or arylalkyl and ~~R_3~~ R_3' is hydrogen, alkyl, arylalkyl or acyl.

Q is hydrogen, linear, branched or cyclic alkyl or aryl, provided that when P is hydrogen, Q is not hydrogen;
and pharmaceutically acceptable salts thereof.

21. (Previously Presented) The compound of claim 20, wherein Z is –C(O)- or C_1-C_4-alkylene-C(O)-.

22. (Original) The compound of claim 21, wherein Z is -C(O)- or C_1-C_2-alkylene-C(O)-.

23. (Cancelled)

24. (Cancelled)

25. (Previously Presented) The compound of claim 20, wherein Z is C_1-C_6-alkylene-O- or C_1-C_6-alkylene-NR-.

26. (Original) The compound of claim 25, wherein Z is C_1-C_4-alkylene-O- or C_1-C_4-alkylene-NH-.

27. (Original) The compound of claim 26, wherein Z is C_1-C_2-alkylene-O- or C_1-C_2-alkylene-NH.

28. (Currently Amended) The compound of claim 25, wherein Q is hydrogen, linear, branched or cyclic C_1-C_6-alkyl , phenyl or naphthyl, provided that when P is hydrogen or -OR, Q is not hydrogen.

29. (Original) The compound of claim 28, wherein Q is isopropyl, phenyl or cyclohexyl.

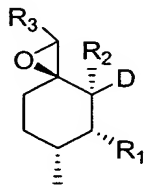
30. (Original) The compound of claim 20, wherein each R is, independently, hydrogen or linear, branched or cyclic C_1-C_6-alkyl.

31. (Original) The compound of claim 30, wherein each R is, independently, hydrogen or linear or branched C_1-C_4-alkyl.

32. (Original) The compound of claim 31, wherein each R is, independently, hydrogen or methyl.

33. (Original) The compound of claim 32, wherein each R is hydrogen.

34. (Previously Presented) The compound of claim 20, wherein A is of Formula II,



(II)

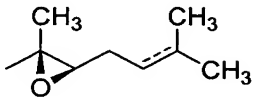
wherein

R_1 is hydrogen or alkoxy;

R_2 is hydrogen or hydroxy;

R_3 is hydrogen or alkyl; and

D is linear or branched alkyl or arylalkyl; or D is of the structure



35. (Original) The compound of claim 34, wherein R_1 is C_1-C_4-alkoxy.

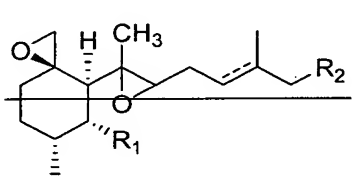
36. (Original) The compound of claim 35, wherein R_1 is methoxy.

37. (Original) The compound of claim 34, wherein R_3 is hydrogen or C_1-C_4-alkyl.

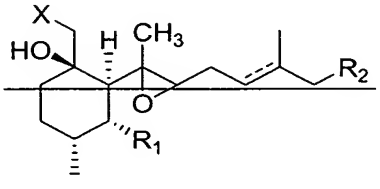
38. (Original) The compound of claim 37, wherein R_3 is methyl.

39. (Previously Presented) The compound of claim 34, wherein D is linear, or branched C_1-C_6-alkyl; or aryl-C_1-C_4-alkyl.

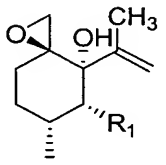
40. (Previously Presented) The compound of claim 20, wherein A is selected from the group consisting of



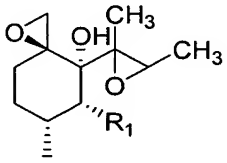
(IV)



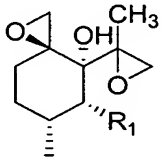
(V)



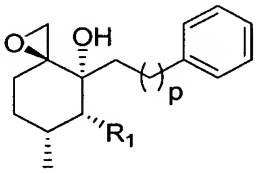
(VI)



(VII)



(VIII)



(IX)

wherein

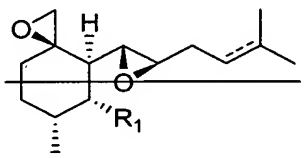
p is an integer from 0 to 10;

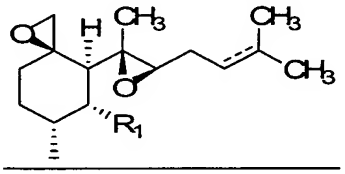
R_1 is hydrogen, -OH or C_1-C_4-alkoxy;

X is a leaving group; and

R_2 is H, OH, amino, C_1-C_4-alkylamino or di(C_1-C_4)-alkylamino.

41. (Currently Amended) The compound of claim 40, wherein A is of the formula





42. (Original) The compound of claim 20, wherein P comprises from 1 to about 20 amino acid residues.

43. (Original) The compound of claim 42, wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

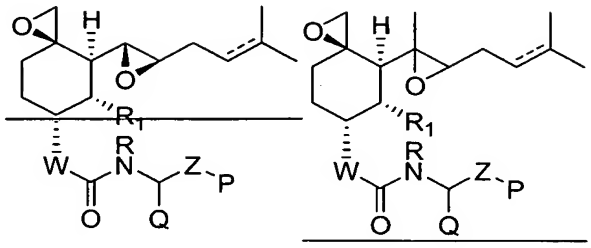
44. (Original) The compound of claim 43, wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

45. (Original) The compound of claim 44, wherein the matrix metalloprotease is MMP-2 or MMP-9.

46. (Original) The compound of claim 45, wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

47. (Currently Amended) The compound of claim 46, wherein P comprises ~~a~~ the sequence ~~selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15);~~ Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16)~~; Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23)~~.

48. (Currently Amended) A compound of the formula



wherein

W is O or NR;

each R is, independently hydrogen or a C_1-C_4-alkyl;

Q is hydrogen~~; linear, branched or cyclic C_1-C_6-alkyl; or aryl;~~

R_1 is hydroxy, C_1-C_4-alkoxy or halogen;

Z is –C(O)- or C_1-C_4-alkylene-C(O)-;

P is ~~NHR, OR, or~~ a peptide comprising 1 to 100 amino acid residues attached to Z at the N-terminus; or

Z is alkylene-O or alkylene-NR; and

P is ~~hydrogen or~~ a peptide comprising 1 to 100 amino acid residues attached to Z at the C-terminus;

or a pharmaceutically acceptable salt thereof~~; provided that when P is hydrogen, NHR or OR, Q is not hydrogen~~.

49. (Cancelled)

50. (Cancelled)

51. (Original) The compound of claim 48, wherein P comprises from 1 to about 20 amino acid residues.

52. (Original) The compound of claim 51, wherein P comprises an amino acid sequence which is a substrate for a matrix metalloprotease.

53. (Original) The compound of claim 52, wherein the matrix metalloprotease is selected from the group consisting of MMP-2, MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-13 and MMP-26.

54. (Original) The compound of claim 53, wherein the matrix metalloprotease is MMP-2 or MMP-9.

55. (Original) The compound of claim 54, wherein P comprises the sequence -Pro-Leu-Gly-Xaa-, wherein Xaa is a naturally occurring amino acid residue.

56. (Currently Amended) The compound of claim 55, wherein P comprises ~~a~~ the sequence ~~selected from the group consisting of Pro-Cha-Gly-Cys(Me)-His (SEQ ID NO:2); Pro-Gln-Gly-Ile-Ala-Gly-Gln-D-Arg (SEQ ID NO:3); Pro-Gln-Gly-Ile-Ala-Gly-Trp (SEQ ID NO:4); Pro-Leu-Gly-Cys(Me)-His-Ala-D-Arg (SEQ ID NO:5); Pro-Leu-Gly-Met-Trp-Ser-Arg (SEQ ID NO:35); Pro-Leu-Gly-Leu-Trp-Ala-D-Arg (SEQ ID NO:6); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:7); Pro-Leu-Ala-Leu-Trp-Ala-Arg (SEQ ID NO:8); Pro-Leu-Ala-Tyr-Trp-Ala-Arg (SEQ ID NO:9); Pro-Tyr-Ala-Tyr-Trp-Met-Arg (SEQ ID NO:10); Pro-Cha-Gly-Nva-His-Ala (SEQ ID NO:11); Pro-Leu-Ala-Nva (SEQ ID NO:12); Pro-Leu-Gly-Leu (SEQ ID NO:13); Pro-Leu-Gly-Ala (SEQ ID NO:14); Arg-Pro-Leu-Ala-Leu-Trp-Arg-Ser (SEQ ID NO:15);~~ Pro-Cha-Ala-Abu-Cys(Me)-His-Ala (SEQ ID NO:16)~~; Pro-Cha-Ala-Gly-Cys(Me)-His-Ala (SEQ ID NO:17); Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu (SEQ ID NO:18); Pro-Lys-Pro-Leu-Ala-Leu (SEQ ID NO:19); Arg-Pro-Lys-Pro-Tyr-Ala-Nva-Trp-Met (SEQ ID NO:20); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:21); Arg-Pro-Lys-Pro-Val-Glu-Nva-Trp-Arg (SEQ ID NO:22); and Arg-Pro-Lys-Pro-Leu-Ala-Nva-Trp (SEQ ID NO:23)~~.

57. (Currently Amended) An angiogenesis inhibitor compound selected from the group consisting of

~~N-Carbamoyl-GlyArgGlyAspSerPro-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArgGlyAspTyr(OMe)ArgGlu-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArgGlyAsp-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R-)2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArgGlyAsp-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArg-{3-amino-3(pyridyl)}-propionic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbomoyl-GlyProLeuGly-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~Ac-ProLeuMetTrpAla-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl}-amino-3-methyl-butanol) ester;~~

~~Ac-ProLeuGlyMet-(2*R*-{(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl}-amino-3-methyl-butanol) ester;~~

~~Ac-ProLeuGlyMetAla-2*R*-{(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yloxycarbonyl}-amino-3-methyl-butanol) ester;~~

{2-Methyl-1-[methyl-(1-methyl-piperidin-4-yl)-carbamoyl]-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(2-Dimethylamino-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

{1-[(2-Dimethylamino-ethyl)-methyl-carbamoyl]-2-methyl-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(3-Dimethylamino-propylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(3-Dimethylamino-2,2-dimethyl-propylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[2-Methyl-1-(4-methyl-piperazine-1-carbonyl)-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

{2-Methyl-1-[2-(1-methyl-pyrrolidin-2-yl)-ethylcarbamoyl]-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[2-Methyl-1-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester; and

[1-(4-Benzyl-piperazine-1-carbonyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester.

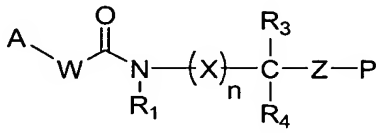
58. (Cancelled)

59. (Cancelled)

60. (Cancelled)

61. (Cancelled)

62. (Currently Amended) A method of treating an angiogenic disease in a subject, comprising administering to the subject a therapeutically effective amount of an angiogenesis inhibitor compound comprising the structure



wherein

A is a Met-AP2 inhibitory core;

W is O or NR_2;

R_1 and R_2 are each, independently, hydrogen or alkyl;

X is alkylene or substituted alkylene;

n is 0 or 1;

R_3 and R_4 are each, independently, ~~hydrogen,~~ substituted ~~or unsubstituted~~ alkyl, substituted ~~or unsubstituted~~ aryl or substituted or unsubstituted heteroaryl; or R_3 and R_4, together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or R_3 and R_4 together form an alkylene group;

Z is -C(O)-, alkylene or alkylene-C(O)-; and

P is a peptide comprising from 1 to about 100 amino acid residues attached at its amino terminus to Z or a group OR_5 or $N(R_6)R_7$, wherein

R_5, R_6 and R_7 are each, independently, hydrogen, alkyl, substituted alkyl, azacycloalkyl or substituted azacycloalkyl; or R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic ring structure;

or

Z is -O-, $-NR_8$-, alkylene-O- or alkylene-NR_8-, where R_8 is hydrogen or alkyl; and

P is hydrogen or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z; wherein

the N-terminus of the peptide is $-NR_2'R_3'$, wherein R_2' is hydrogen, alkyl or arylalkyl and R_3' is hydrogen, alkyl, arylalkyl or acyl.

63. (Original) The method of claim 62, wherein said angiogenic disease is an autoimmune disease.

64. (Original) The method of claim 63, wherein said autoimmune disease is rheumatoid arthritis.

65. (Original) The method of claim 62, wherein said angiogenic disease is cancer.

66. (New) The compound of claim 1, wherein R_1 is a substituted or unsubstituted alkyl group.

67. (New) The compound of claim 66, wherein R_1 is a substituted or unsubstituted normal, branched or cyclic C_1-C_6 alkyl group.

68. (New) The compound of claim 67, wherein R_1 is a normal or branched C_1-C_4 alkyl group.